arginase deficiency

Arginase deficiency is an inherited disorder that causes the amino acid arginine (a building block of proteins) and ammonia to accumulate gradually in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

Arginase deficiency usually becomes evident by about the age of 3. It most often appears as stiffness, especially in the legs, caused by abnormal tensing of the muscles (spasticity). Other symptoms may include slower than normal growth, developmental delay and eventual loss of developmental milestones, intellectual disability, seizures, tremor, and difficulty with balance and coordination (ataxia). Occasionally, high protein meals or stress caused by illness or periods without food (fasting) may cause ammonia to accumulate more quickly in the blood. This rapid increase in ammonia may lead to episodes of irritability, refusal to eat, and vomiting.

In some affected individuals, signs and symptoms of arginase deficiency may be less severe, and may not appear until later in life.

Frequency

Arginase deficiency is a very rare disorder; it has been estimated to occur once in every 300,000 to 1,000,000 individuals.

Genetic Changes

Mutations in the *ARG1* gene cause arginase deficiency.

Arginase deficiency belongs to a class of genetic diseases called urea cycle disorders. The urea cycle is a sequence of reactions that occurs in liver cells. This cycle processes excess nitrogen, generated when protein is used by the body, to make a compound called urea that is excreted by the kidneys.

The *ARG1* gene provides instructions for making an enzyme called arginase. This enzyme controls the final step of the urea cycle, which produces urea by removing nitrogen from arginine. In people with arginase deficiency, arginase is damaged or missing, and arginine is not broken down properly. As a result, urea cannot be produced normally, and excess nitrogen accumulates in the blood in the form of ammonia. The accumulation of ammonia and arginine are believed to cause the neurological problems and other signs and symptoms of arginase deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- ARG1 deficiency
- Arginase Deficiency Disease
- Argininemia
- Hyperargininemia

Diagnosis & Management

These resources address the diagnosis or management of arginase deficiency:

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/argininemia
- GeneReview: Arginase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1159
- GeneReview: Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217
- Genetic Testing Registry: Arginase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268548/
- MedlinePlus Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm
- National Organization for Rare Disorders (NORD) Physician Guide: Urea Cycle Disorders
  http://nordphysicianguides.org/urea-cycle-disorders/
- New England Consortium of Metabolic Programs: Acute Illness Protocol
  http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/arginase-deficiency/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html

- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm
- Health Topic: Amino Acid Metabolism Disorders
  https://medlineplus.gov/aminoacidmetabolismdisorders.html
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Arginase deficiency
  https://rarediseases.info.nih.gov/diseases/5840/arginase-deficiency

Educational Resources

- Cincinnati Children's Hospital
  https://www.cincinnatichildrens.org/health/u/ucd
- Connecticut Department of Public Health
  http://www.ct.gov/dph/lib/dph/family_health/newborn_screening/pdf/argininemia_hp.pdf
- Disease InfoSearch: Arginase Deficiency
  http://www.diseaseinfosearch.org/Arginase+Deficiency/574
- Genetics Education Materials for School Success (GEMSS)
  http://www.gemssforschools.org/conditions/urea-cycle/default
- MalaCards: argininemia
  http://www.malacards.org/card/argininemia

- Orphanet: Argininemia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=90
- Screening, Technology and Research in Genetics
  http://www.newbornscreening.info/Parents/aminoaciddisorders/argininemia.html

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/arginase-deficiency/
- National Urea Cycle Disorders Foundation
  http://www.nucdf.org/
- Urea Cycle Disorders Consortium
  http://www.rarediseasesnetwork.org/cms/UCDC

GeneReviews

- Arginase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1159
- Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217

Genetic Testing Registry

- Arginase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268548/

ACT Sheets

- Increased Arginine
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Arginine.pdf

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22arginase+deficiency%22+OR+%22Hyperargininemia%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28arginase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- ARGININEMIA
  http://omim.org/entry/207800

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